# Cardiovascular medication use after coronary bypass surgery in patients with renal dysfunction: A national Veterans Administration study<sup>1</sup>

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## Cardiovascular medication use after coronary bypass surgery in patients with renal dysfunction: A national Veterans Administration study.

Background. Chronic kidney disease is now recognized as an independent risk factor for cardiovascular events. We sought to determine if cardiovascular medications were utilized less in patients with renal dysfunction following coronary artery bypass grafting (CABG) and if the association of decreased medication use was independent of comorbid conditions. We also examined associations between cardiovascular medication use and mortality at 6 months.

Methods. Data from the National Veterans Adminstration (VA) Continuous Improvement in Cardiac Surgery Program were merged with the national VA pharmacy database. Prescription rates within 6 months of discharge for CABG were obtained for four classes of medicines: beta blockers, lipid-lowering agents, antiplatelet agents, and angiotensin antagonists. Utilization of medications in patients with estimated glomerular filtration rate (GFR) 60 to 90, 30 to 60, and <30 were compared with the reference group of GFR >90.

Results. In a retrospective analysis of 19,411 patients, the frequency of nonprescription increased with declining GFR. Decreased utilization for patients with GFR 30 to 60 and <30 remained highly significant after adjustment for age, race, hypertension, diabetes, and prior myocardial infarction. In patients with more advanced renal dysfunction (GFR <60), cardiovascular medication use for all medication classes was associated with survival at 6 months after adjusting for demographic and

<sup>1</sup>This is a U.S. Government work. There are no restrictions on its use.

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utilization of cardiovascular medications. Nonprescription of medications was associated with adverse outcomes in those with renal dysfunction.

medication from each additional class.

clinical variables. Cumulative protection was seen with use of

renal disease is associated with highly significant decreases in

Conclusion. In a large VA population undergoing CABG,

Chronic kidney disease has recently been recognized as an important independent risk factor for cardiovascular events and death from cardiovascular disease. The risk of cardiovascular disease in chronic kidney disease is not fully explained by the presence of multiple risks, including hypertension, diabetes, older age, dyslipidemia, and a high burden of left ventricular hypertrophy (LVH). Given this information, the National Kidney Foundation has recommended that patients with chronic kidney disease be classified as a cardiovascular disease equivalent [1, 2]. Despite the growing frequency of chronic kidney disease and adverse cardiac outcomes, recognition, prevention, and treatment of cardiovascular disease in this patient population are often poor. In many settings, chronic kidney disease has been associated with decreased utilization of key cardiovascular medications. In patients who sustain myocardial infarction or have confirmed cardiovascular disease, patients receiving chronic dialysis and those with chronic kidney disease have been shown to have comparatively lower use of aspirin, angiotensinconverting enzyme (ACE) inhibitors, beta blockers, 3-hydroxy-3-methylglutaryl coenzymeA (HMG-CoA) reductase inhibitors, glycoprotein IIb/IIIa inhibitors, and

angiography [3–12]. Despite frequent exclusion from randomized controlled trials of cardiovascular agents,

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patients with chronic kidney disease of various forms have been shown to benefit from cardiovascular medications in randomized controlled trials. For example, studies of beta blockers have shown reductions in mortality in end-stage renal disease (ESRD) patients with cardiomy-opathy [13], studies of angiotensin receptor blockers have lowered cardiovascular events in patients with type 2 diabetes and nephropathy [14], and studies of statins have demonstrated reductions in cardiovascular events in patients receiving kidney transplants [15].

Following coronary artery bypass grafting (CABG), prevention and treatment of underlying cardiovascular disease may have particular relevance. Specifically, CABG may address the challenges posed by anatomic lesions of coronary artery disease, but does not remediate the underlying disease process, atherosclerotic disease. Here, secondary prevention with cardiovascular medications may prove beneficial [16, 17]. For lipid-lowering agents, there are strong data supporting use after CABG [18]. Aspirin, beta blockers, and angiotensin antagonists are likely beneficial in improving graft patency, prevention of atrial fibrillation, and in those with left ventricular dysfunction [19-21]. ACE inhibitors are also beneficial in unselected patients with atherosclerosis, with or without low ejection fraction [22]. Mortality benefits for these agents after CABG are suggested but have not yet been rigorously proven [17].

Because preexisting kidney disease has been demonstrated to be a predictor of adverse outcomes after CABG [23], it seems logical to examine the chronic kidney disease population as a target for improving chronic kidney disease-specific and overall outcomes in cardiac surgery. Since the causes of underutilization in chronic kidney disease remain poorly understood [24], and there are no existing data on utilization of medications after CABG in patients with chronic kidney disease, this area represents a great knowledge deficit, especially in the United States Veterans population. Our study aims were to determine if chronic kidney disease is associated with lower cardiovascular medication use after CABG in the Veterans Administration (VA) population and if factors explaining lower prescription rates can be explained by demographic or clinical factors. Given the lack of data for chronic kidney disease patients in randomized controlled trials of cardiovascular medications, we also hoped to determine if cardiovascular medication use in patients with chronic kidney disease is associated with improved 6-month survival after CABG.

#### **METHODS**

#### Study subjects and data collection

The VA Continuous Improvement in Cardiac Surgery (CICSP) clinical data have been collected since 1987 on all patients undergoing cardiac surgery in the VA hos-

pitals. Trained surgical clinical nurse reviewers at each of the 43 cardiac surgical centers collect preoperative risk factors, procedural details, and outcomes. The CI-CSP database is reliable and accurate and has been employed successfully by other investigators [25]. From the CICSP database, deidentified records for CABG procedures performed between October 1, 1999 and March 31, 2003 were extracted for this retrospective analysis. For the purposes of this study, valve procedures and repeat operations were excluded. Because patients not surviving to discharge were ineligible to receive prescriptions, patients with in-hospital death were also excluded. The study population consisted of 19,411 subjects receiving CABG and surviving to hospital discharge.

To obtain prescription fill rates, the CICSP data were merged with the VA Pharmacy Benefits Management Prescription Database (PBM) as part of the ongoing quality improvement reporting initiatives within the VA system. The PBM database contains information on all pharmaceutical agents prescribed and filled in the VA system. This comprehensive system is updated monthly. For the analysis, four classes of drugs were selected for extraction: antiplatelet agents, beta blockers, lipid-lowering agents, and angiotensin antagonists. Antiplatelet agents included aspirin, clopidogrel, dipyridamole, ticlopidine, and other aspirin substitutes. Beta blockers included nonselective and selective agents, as well as agents with intrinsic sympathomimetic activity. Lipid-lowering agents included statins and nonstatin agents, and angiotensin antagonists included ACE inhibitors and angiotensin receptor blockers.

Classification of patients into classes of renal functional decline by estimated glomerular filtration rate (GFR) was performed according to the formula of Cockroft and Gault using the admission presurgery serum creatinine value [26]. Race was unknown or missing for 3958 patients, preventing use of the newer Modification of Diet in Renal Disease (MDRD) Study equation for estimation of GFR [27]. For analysis of the association between GFR and nonprescription, patients with GFR >90 were used as the reference group. Clinical and demographic variables were also extracted for baseline comparisons and for multivariate analysis.

#### **Study outcomes**

The primary outcome of interest was nonprescription within 6 months of discharge for each class of cardio-vascular medication. Patients with GFR <30, GFR 30 to 60, and GFR 60 to 90 were compared with the reference group of GFR >90. Nonprescription was defined as the failure to fill any prescription for a class of medication at any VA pharmacy within 6 months of discharge. Discharge medications were included as prescriptions. Prescriptions filled outside the VA system were not recorded.

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Glomerular filtration rate	>90	60 to 90	30 to 60	<30	P value <sup>a</sup>
Number (%)	8122 (41.8)	7236 (37.3)	3661 (18.9)	392 (2.0)	
Age (mean $\times$ SD)	$58 \times 7.7$	$66 \times 8.2$	$72 \times 7.6$	$67 \times 10.3$	< 0.0001
Black race%	6.2	7.2	8.9	15.5	< 0.0001
Hypertension%	82.8	85.6	88.7	92.7	< 0.0001
Diabetes%	39.8	35.7	37.0	54.1	0.31
Prior myocardial infarction%	54.9	55.5	61.0	65.1	< 0.0001
Left ventricular ejection fraction <40%%	11.4	12.2	16.0	19.4	< 0.0001
Chronic obstructive pulmonary disease%	22.2	24.4	29.3	26.3	< 0.0001

**Table 1.** Baseline characteristics of the Veterans Administration Continuous Improvement in Cardiac Surgery (VA CICSP) Study Population (N = 19.411)

The 6-month time limit was chosen because some veterans receive medications in 6-month increments, and preoperative medications would need to be refilled by that time limit. The secondary outcome of interest was the association between cardiovascular medication use and all-cause mortality at 6 months in patients with advanced renal decline (GFR <60). We also explored the incidence of renal impairment in the study population and the association between renal impairment and the risk of all-cause mortality at 6 months. Mortality within 30 days was captured by CICSP study nurses; other mortalities and dates of death were captured by the Veterans Administration "BIRLS" database which tracks the administration of death benefits.

#### Statistical analysis

Baseline variables were compared using the Cochran-Mantel-Haenszel Chi-square for categoric variables and analysis of variance (ANOVA) for continuous variables. Hypertension, prior myocardial infarction, chronic obstructive pulmonary disease (COPD), and diabetes were classified as binomial variables. Race was classified as African American or non-African American.

Multivariate logistic regression was performed to determine the effect of GFR on the rate of nonprescription of antiplatelet agents, beta blockers, lipid-lowering agents, and angiotensin antagonists. For beta blockers, patients with COPD were excluded from the analysis. For angiotensin antagonists, the analysis was repeated using those patients with left ventricular ejection fraction (LVEF) <40%, as this group has the most widely recognized indication to receive angiotensin antagonists. Multivariate analysis was adjusted for patient age, race, hypertension, diabetes, prior myocardial infarction, and each of the individual medication classes.

To determine if secondary prevention appeared beneficial, we used logistic regression to analyze if medication use from the above classes was associated with improved survival at 6 months. This was performed in patients with and without advanced renal impairment (GFR <60). Patients who died within 30 days of surgery were excluded, as they would not have had an opportunity to fill any

outpatient prescriptions. We also analyzed the effects of using multiple classes of cardiovascular medications on 6-month mortality. The analysis of the effect of medication use on 6-month mortality was adjusted for patient age, race, hypertension, diabetes, baseline serum albumin, and baseline serum creatinine. All analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC, USA).

As part of the VA Continuous Improvement in Cardiac Surgery Program's initiative to explore opportunities to improve processes of care for CABG patients, this study subanalysis was incorporated into the Colorado Multiple Institutional Review Board (COMIRB) approval. As appropriate for records received since April 2003, a Health Insurance Portability and Accountability Act (HIPAA) waiver of authorization was obtained.

#### **RESULTS**

Baseline characteristics of the study population and distribution according to GFR are found in Table 1. Information for analysis was available for 19,411 patients. 99% of whom were male. Renal functional impairment, defined by a GFR < 90, was present in the majority of the study population (58.2%). Advanced renal impairment, defined as GFR <60, was found in 20.9% of the population. Hypertension was present in 85% of patients, and prior myocardial infarction had occurred in 54.5%. Diabetes and COPD were also common, occurring in 38% and 24.5%, respectively. In addition, 12.7% had an ejection fraction (EF) less than 40%, and 7.2% were classified as African American. While most variables showed statistically significant differences among GFR groups at baseline due to the large numbers of patients, clinically significant differences existed. Patients with renal disease tended to be older, were more likely to be black, and had higher incidences of hypertension, prior myocardial infarction, EF <40%, and COPD. Over 50% of patients with GFR <30 had a diagnosis of diabetes.

The frequencies of study endpoints (nonprescription, 6-month mortality) stratified by GFR are found in Table 2. For each class of agents, a highly significant, stepwise decrease in the rate of utilization was seen as kidney

<sup>&</sup>lt;sup>a</sup>Chi-squared Mantel-Haenszel for categoric variables; analysis of variance (ANOVA) for continuous variables.

**Table 2.** Frequency of study end points: Nonprescription and mortality by glomrular filtration rate (GFR) group

GFR	All	>90	60 to 90	30 to 60	<30	P value <sup>a</sup>
Antiplatelet agents%	18.0	16.2	17.3	22.5	26.0	< 0.0001
Lipid-lowering agents%	20.7	16.2	20.6	29.1	39.0	< 0.0001
Beta blockers <sup>a</sup> %	12.3	8.4	11.4	14.7	20.8	< 0.0001
Angiotenin antagonists%	39.0	38.3	38.3	41.3	46.9	< 0.0002
6-month mortality%	4.7	2.7	4.2	9.0	13.5	< 0.0001

<sup>a</sup>Patients with chronic obstructive pulmonary disease excluded for beta blockers.

function declined. For angiotensin antagonists, these differences were not seen in the GFR 60 to 90 vs. the reference group. However, for all other GFR groups and each of the four medication classes, there were statistically significant decreases in utilization with each advancing stage of kidney disease. We also verified previous findings of the effect of presurgery GFR on outcomes. GFR powerfully predicted mortality at 6 months (P < 0.0001), with 13.5% of patients in the GFR <30 group experiencing mortality after surviving to discharge. This rate declined to 9.0%, 4.1%, and 2.7% in the GFR 30 to 60, 60 to 90, and >90 groups, respectively. The results for Tables 3 and 4 will be discussed below for each class of medication. In Table 5, we demonstrate the cumulative effect of receiving cardiovascular medications on the odds of mortality at 6 months. Specifically, the odds of mortality at 6 months decrease dramatically with prescription of medications from each additional class. This apparent benefit is seen in patients with and without GFR <60.

#### **Antiplatelet agents**

A total of 18% of patients in the CICSP study did not receive any antiplatelet agent from a VA pharmacy within 6 months of discharge. These gross rates are likely influenced by over-the-counter purchase of aspirin outside VA sources. However, a strong influence of GFR was seen on the odds of nonprescription. The unadjusted odds of nonprescription were significantly higher for each GFR group when compared to the reference group. After adjusting for patient age, hypertension, race, prior myocardial infaction, diabetes, and use of other cardiovascular medications, the odds of nonprescription was not significantly different among GFR groups. We found that of all the factors included in the analysis, adjustment for other medications erased the univariate differences in prescription among GFR groups. Thus, it appears that prescription of other cardiovascular agents strongly affects prescription of antiplatelet agents within various GFR categories. In those patients with GFR <60 (Table 4), nonprescription of antiplatelet agents was associated with a highly significant increase in the odds of death at 6months. Adjusting for age, hypertension, diabetes, serum creatinine, serum albumin, and race did not change the highly significant nature of the association between non-prescription and death (OR 1.90, P = 0.004).

#### **Beta blockers**

After excluding 4746 patients with COPD, beta blockers were not prescribed in 12.3% of patients. Again, the presence of renal impairment was highly associated with decreased utilization. Only 8.4% of those with GFR >90 did not receive beta blockers. This rate rose to 11.4%, 15%, and 21% in those with GFR 60 to 90, 30 to 60, and <30. The adjusted odds of nonprescription was statistically significant for the GFR 60 to 90 and GFR <30 groups compared with the reference group. There was a strong association seen between nonprescription of beta blockers and increased odds of mortality at 6 months. This association remained highly significant (OR 3.04, P < 0.0001) even after adjusting for age, hypertension, diabetes, serum creatinine, serum albumin, race, and use of other cardiovascular medications.

#### **Lipid-lowering agents**

Lipid-lowering agents were not prescribed in 20.7% of the study population. In those with GFR >90, only 16% did not receive any lipid-lowering agent. With each advancing stage of renal impairment, rates of nonprescription rose to 21%, 29%, and 39%. The unadjusted odds of nonprescription was highly significant in each of the GFR groups, while the adjusted odds of nonprescription were statistically significant in the GFR <30 and GFR 30 to 60 groups; these differences increased in magnitude as kidney function declined (Table 3). Nonprescription of lipid-lowering agents was associated with a highly significant increase in mortality at 6 months in the adjusted analyses in those with advanced renal impairment (GFR <60). The adjustment for serum albumin makes it unlikely that lipid-lowering agents were not prescribed due to malnutrition in patients with kidney disease.

#### **Angiotensin antagonists**

Angiotensin antagonists (ACE inhibitors and angiotensin receptor blockers) were not prescribed in 39% of the study population, and were not prescribed in 27.8% of the 2472 patients with LVEF <40%. Again, the gross rates of nonprescription increased as kidney function declined, except for those with GFR 60 to 90. The unadjusted and adjusted odds of nonprescription were highly significant in those with GFR 30 to 60 and <30. This relationship was even stronger for the patients with LVEF <40% (Table 3). For example, those with GFR <30 and EF<40% had an adjusted odds of nonprescription of 2.83 (P < 0.001). Again, failure to receive angiotensin

**Table 3.** Associations between glomerular filtration rate (GFR) category and odds of nonprescription

	GFR 60 to 90	GFR 30 to 60	GFR <30
Antiplatelet agent			
OR <sup>a</sup> (95% CI)	0.88 (0.80-0.98)	0.97 (0.85–1.10)	1.07 (0.82–1.39)
P value	0.01	0.62	0.62
Lipid-lowering agent			
OR <sup>a</sup> (95% CI)	1.04 (0.95–1.15)	1.28 (1.13–1.44)	2.08 (1.63–2.65)
P value	0.41	< 0.0001	< 0.0001
Beta blockers			
OR <sup>a</sup> (95% CI)	1.20 (1.04–1.39)	1.16 (0.96–1.40)	1.49 (1.05–2.12)
P value	0.01	0.11	0.02
Angiotensin antagonists			
OR <sup>a</sup> (95% CI)	1.01 (0.94–1.09)	1.15 (1.04–1.27)	1.50 (1.20–1.88)
P value	0.76	0.008	< 0.001
Angiotensin antagonist, ejection fraction <40%			
OR <sup>a</sup> (95% CI)	1.08 (0.84–1.39)	1.62 (1.19–2.19)	2.83 (1.64-4.91)
P value	0.56	0.002	< 0.001

<sup>&</sup>lt;sup>a</sup>Variables included age, diabetes, hypertension, race, prior myocardial infarction, and each cardiovascular medication class; GFR >90 is reference.

**Table 4.** Relationship of medication nonprescription to 6-month mortality in patients with and without advanced renal disease [glomerular filtration rate (GFR) < 60]

[8			
	GFR $<$ 60 ( $N = 3260$ )	GFR > 60 ( $N = 12,396$ )	
Failure to receive			
Antiplatelet agents			
OR <sup>a</sup> (95% CI)	1.90 (1.23–2.94)	2.00 (1.37-2.91)	
P value	0.004	< 0.001	
Lipid-lowering agents			
OR <sup>a</sup> (95% CI)	3.69 (2.36–5.77)	3.44 (2.36–5.01)	
P value	< 0.0001	< 0.0001	
Beta blockers			
OR <sup>a</sup> (95% CI)	3.04 (1.94–4.76)	3.43 (2.34–5.03)	
P value	< 0.0001	<0.0001	
Angiotensin antagonists			
OR <sup>a</sup> (95% CI)	1.77 (1.14–2.76)	2.02 (1.40-2.92)	
P value	0.01	<0.001	

<sup>&</sup>lt;sup>a</sup>Variables included age, race hypertension, diabetes, creatinine, serum albumin, and each cardiovascular medication class. Patients who died within 30 days of surgery were excluded.

antagonists after discharge was associated with substantial increase in the odds of 6-month mortality, even after adjustment for age, race, hypertension, diabetes, serum creatinine, serum albumin, and other cardiovascular medications.

#### **DISCUSSION**

Our study provides important new information linking the presence of renal impairment with decreased utilization of important cardiovascular medications after CABG. Although other unmeasured factors (such as medication use outside of the VA health care system) may have influenced the observed medication fill rates, the graded relationship between nonprescription of each agent and advancing renal decline provides enhanced support that this is a true association. Furthermore, we also found that these associations between medication underutilization and GFR were retained af-

**Table 5.** Cumulative protective effect of cardiovascular medications on 6-month mortality in patients with and without advanced renal disease [glomerular filtration rate (GFR) < 60]

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	GFR <60	GFR >60		
Three medications <sup>a</sup> number	1398	5807		
OR <sup>a</sup> (95% CI)	2.48 (1.24-4.94)	1.20 (0.72-2.00)		
P value	0.01	0.49		
Two medications <sup>a</sup> number	566	1852		
OR <sup>a</sup> (95% CI)	6.54 (3.26–13.15)	3.88 (2.32-6.49)		
P value	< 0.0001	< 0.0001		
Onr medication <sup>a</sup> number	150	379		
OR <sup>a</sup> (95% CI)	15.29 (7.01–33.35)	6.56 (3.24–13.30)		
P value	< 0.0001	< 0.0001		
Zero medications <sup>a</sup> number	395	569		
ORa (95% CI)	39.00 (20.79–73.18)	36.19 (23.38-56.03)		
P value	< 0.0001	< 0.0001		

<sup>a</sup>Variables included age, race, hypertension, diabetes, creatinine, serum albumin.HTN, Reference was patients who received cardiovascular medications from all four classes.

ter adjustment for demographic and clinical factors such as age, race, hypertension, diabetes, and prior myocardial infarction. Given the completeness and quality of the CICSP national quality improvement database, the relevance of underutilization in the setting of chronic kidney disease is dramatically underscored by our data defining the incidence and outcomes of renal impairment in the VA CABG population. Specifically, we have shown that among patients undergoing CABG, the majority (58%) of patients had some degree of renal functional impairment, and that fully 21% had GFR <60. While others have shown that events increase in patients with higher values of serum creatinine [23], our study provides conclusive information that as kidney function declines, there is a highly significant increase in the risk of mortality at 6 months, even after excluding those who died prior to discharge.

This study also suggests that as in patients with normal or slightly reduced GFR, patients with GFR <60 benefit from receiving cardiovascular medications after

CABG, an association which has not been previously demonstrated. The greater odds of death at 6 months in patients with GFR <60 who failed to receive each class of medication and the dramatically increased survival when patients received medications from each additional class underscored this point. While associations between medication use and decreased risk of death were observational in nature, the strong relationship and persistence after multivariate adjustment argue that chronic kidney disease patients are probably helped, and are likely not harmed, by cardiovascular medications.

In addition to documenting the presence of underutilization of cardiovascular medication in the chronic kidney disease population, our data also make a compelling argument that disparities in utilization should be eliminated. While reasons may exist for decreased utilization, such as bleeding complications for aspirin, hyperkalemia for ACE-inhibitors, and myopathy for statins, the high risk of cardiovascular events in the chronic kidney disease population should render these side effects less important. For example, the 9.0% and 13.5% risk of death at 6 months in patients with GFR 30 to 60 and <30 in our study probably outweighs the 1.9% risk of serious hyperkalemia with angiotensin receptor blockers seen in large trials of patients with chronic kidney disease [28], although extensive safety data does not exist for patients with GFR <30 due to their exclusion from clinical trials. Similarly, occasional myopathy and rare (<1%)clinically important creatinine kinase elevations are not an adequate explanation for nonprescription of statins, given our data on apparent protection in all patients and prospective data in the general CABG population [18, 29]. While we remain unable to explain the apparent therapeutic disconnect between the extremely high-risk chronic kidney disease population and routine use of secondary prevention, we hope that this study will highlight and begin to reverse the unfortunate trend of undermedicating and undertreating chronic kidney disease patients with cardiovascular agents.

The strengths of this study are the large number of patients, the complete nature of the dataset [25], and the ability to link demographic and clinical factors with comprehensive pharmacy information and patient outcomes. In the United States, this sort of information is not frequently available except in large managed care organizations [30]. Because the study captured all patients receiving CABG in the VA system, it is has the potential ability to raise similar questions that may be faced by other national health insurance programs (e.g., Medicare) or international health program (e.g., Canadian or other national health care system). Other strengths include the ability to adjust for multiple factors that may affect prescription rates and outcomes.

Despite the comprehensive nature of the dataset, there are limitations inherent in any observational or retro-

spective study design. Risk adjustment may not equivalently account for differences in patients with advancing degrees of chronic kidney disease; thus, our study does not prove that renal disease is the causative factor in decreased utilization of cardiovascular medications, nor does it prove that decreased utilization is the causative factor behind decreased survival in those who fail to receive cardiovascular medications. However, our primary focus was not to prove causation, but to identify gaps in clinical care that could serve as future quality improvement targets. The PBM data on prescription information is limited by the extent that patients may fill their medications outside the VA system. It is unknown to what degree veterans utilized prescription drug benefits through another insurance system (e.g., their state-based Medicaid program provided pharmacy coverage). Also, if aspirin, niacin, or other low-cost medication can be obtained over the counter at a lower cost, patients may purchase medications outside the VA. It is likely that veteran use of external pharmacy services affects aggregate rates of nonprescription, however, but fails to explain large differences in patients with renal impairment or improved outcomes in those who receive medications. We also did not assess regional or physician-specific variation in this study, which may be a topic of further investigation. Compliance (patients who received prescriptions but did not fill them) was not measured either, which limits our conclusions. Additionally, unmeasured patient risk factors (e.g., clinical contraindications to cardiovascular medications) are not measured in this study. Finally, any VA study is limited to the extent that the veterans are not generally representative of the United States population. However, our group has previously published data that showed similar utilization of cardiovascular medications in the post-CABG cohort when compared with other populations [31]. Thus, we believe our results are likely to correspond to other populations receiving CABG.

#### **CONCLUSION**

Renal impairment existed to some degree in the majority of the VA population undergoing CABG and was strongly associated with decreased use of key cardiovascular medications. These differences in prescription were not fully explained by demographic or clinical factors. Furthermore, our data suggest that patients with renal disease likely derive substantial benefit from cardiovascular medications. Since the presence of advancing renal functional decline was a powerful predictor of adverse outcomes, quality and prevention efforts in chronic kidney disease should be refocused on secondary prevention with cardiovascular medications after CABG and in other cardiovascular disease settings.

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Q3

### Queries

**Q1** Author: City and state ok.

**Q2** Author: please provide dates.

**Q3** Author: Please supply the authors to reference 29.